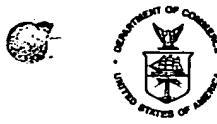


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UNITED STATES PATENT AND TRADEMARK OFFICE  
Address: COMMISSIONER OF PATENTS AND TRADEMARKS  
Washington, D.C. 20231

08/466,554	APPLICATION NUMBER	FILING DATE	FIRST NAMED APPLICANT	ATTORNEY DOCKET NO.
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08/466,554 06/06/95 SEUBERT

P 15270-002120

EXAMINER

18M1/0514

JEAN M. DUVALL  
ATHENA NEUROSCIENCES  
800 GATEWAY BLVD.  
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DUFFY, P. ART UNIT PAPER NUMBER

21

1818

DATE MAILED:

05/14/97

This is a communication from the examiner in charge of your application.  
COMMISSIONER OF PATENTS AND TRADEMARKS

### OFFICE ACTION SUMMARY

Responsive to communication(s) filed on 12-20-96  
 This action is FINAL.  
 Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire three month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

#### Disposition of Claims

Claim(s) 41-47 is/are pending in the application.  
Of the above, claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 Claim(s) \_\_\_\_\_ is/are allowed.  
 Claim(s) 41-47 is/are rejected.  
 Claim(s) \_\_\_\_\_ is/are objected to.  
 Claims \_\_\_\_\_ are subject to restriction or election requirement.

#### Application Papers

See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.  
 The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.  
 The proposed drawing correction, filed on \_\_\_\_\_ is  approved  disapproved.  
 The specification is objected to by the Examiner.  
 The oath or declaration is objected to by the Examiner.

#### Priority under 35 U.S.C. § 119

Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).  
 All  Some\*  None of the CERTIFIED copies of the priority documents have been received.  
 received in Application No. (Series Code/Serial Number) \_\_\_\_\_  
 received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

\*Certified copies not received: \_\_\_\_\_

Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

#### Attachment(s)

Notice of Reference Cited, PTO-892  
 Information Disclosure Statement(s), PTO-1449, Paper No(s). Aug 30, 1996, December 26, 1996,  
 Interview Summary, PTO-413  
 Notice of Draftsperson's Patent Drawing Review, PTO-948  
 Notice of Informal Patent Application, PTO-152

- SEE OFFICE ACTION ON THE FOLLOWING PAGES -

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***Response to Amendment***

1. The amendment filed December 20, 1996 has been entered into the record. Claims 42-47 are pending and under examination.
2. The Group and/or Art Unit of U.S. Patent application SN 08/466,554 has changed. In order to expedite the correlation of papers with the application please direct all future correspondence to Group 1800, Art Unit 1818.
3. The rejection of claims 41-47 under 35 USC, 112 first paragraph is withdrawn based on applicants amendments, declaration and arguments.

***New Rejections***

***Claim Rejections - 35 USC § 102 or 103***

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371 of this title before the invention thereof by the applicant for patent.

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

- (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

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having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 41-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over McConlogue et al (U.S. Patent 5,612,486) in view of Marotta et al (U.S. Patent 5,547,841), Suzuki et al (Science 264:1336-1340, 1994), Vigo-Pelfrey et al (Journal of Neurochemistry, 61(5):1965-1968, 1993).

McConlogue et al teach transgenic mice expressing the Swedish mutation. McConlogue et al teach that the effect of test compounds may be determined by analyzing the effect of the compound on the production of the amino terminal fragment of  $\beta$ APP (ATF- $\beta$ APP) in a variety of biological fluids from the test animals including blood and cerebrospinal fluid. McConlogue et al teach that "In all cases, it will be necessary to obtain a control value which is characteristic of the level of ATF- $\beta$ APP in the test animal in the absence of the test compound(s)." (column 12, last full paragraph). McConlogue et al teaches an *in vivo* screening assay to screen for compounds which alter the amount of ATF- $\beta$ APP, in test specimens of the Swedish transgenic mouse by obtaining a ATF- $\beta$ APP reference value as a control (i.e. the instant first amount), administering the test compound and examining the amount of ATF- $\beta$ APP and determining deviation from the control value. The test agents can be any molecule, compound or other substance which can

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be administered to the test animal and are administered at typical dosages of 1 ng/kg to 10 mg/kg (column 13, first full paragraph). McConlogue et al differ by not testing for A $\beta$  (x->41) in the cerebrospinal fluid.

Marotta et al teach that transgenic mice overexpressing amyloid provide an experimental medium to serve as tools for screening for compounds which may prevent or limit amyloid accumulation either intracellularly or *extracellularly* and that such animal will provide insight into the synthesis and metabolism of amyloid that may have relevance to the over accumulation of amyloid in the brain (see columns 2-3). Marotta et al teach that the mice may be used to evaluate compounds which prevent or limit the production of A4 amyloid or which increase the degradation of amyloid *in vivo* (column 8, second full paragraph). Marotta et al teach that A4 amyloid of the invention includes any A4-amyloid polypeptide from any species and includes any analogue, homologue, mutant or derivative of a naturally occurring homologue and is inclusive of fragments having less than the naturally occurring number of amino acids (column 5).

Suzuki et al teach a sandwich enzyme linked immunosorbent assay which measures A $\beta$ (1-42) in a fluid sample using the combination of the monoclonal antibody BAN50, which specifically binds A $\beta$ (1-16) and the monoclonal antibody BC-05 which was raised to A $\beta$ (33-43) (see pages 1337-1338). Suzuki et al teach that the assay was specific for A $\beta$ (1-42) and does not detect A $\beta$ (1-40) and thus innately measures A $\beta$  (x->41).

Vigo-Pelfrey et al teach that multiple complex forms of A $\beta$  have been isolated and characterized from CSF derived from patients with either meningitis or other neurological disorders (i.e. dementia) including A $\beta$ (1-42). Vigo-Pelfrey et al also teach that A $\beta$  is one of the main components of senile plaques in the brain tissue of Alzheimer's Disease. Vigo-Pelfrey et al teach that amino acid sequencing reveals several soluble species of A $\beta$  and in particular teach

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the species of A $\beta$ (1-42) are present in the CSF of diseased individuals including those with dementia.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modify the screening assay of McConlogue et al by testing for compounds which alter the amount of A $\beta$  (x->41) in the cerebrospinal fluid, in place of ATF- $\beta$ APP, in the Swedish transgenic mouse, using the immunoassay of Suzuki et al which detects A $\beta$  (1-42), by obtaining a A $\beta$  (x->41) reference value as a control (i.e. the instant first amount), administering the test compound and determining a post administration level and examining deviation from the control value (i.e. the instant second amount) because Marotta et al teach that transgenic mice overexpressing amyloid provide an experimental medium to serve as tools for screening for compounds which may prevent or limit amyloid accumulation either intracellularly or *extracellularly* and that such can be used to evaluate compounds which prevent or limit the production of A4 amyloid or which increase the degradation of amyloid *in vivo* and Vigo-Pelfrey et al teach the presence of amyloid peptides in the CSF having 1-42 amino acids and the assay of Suzuki et al would provide a simpler, more economic, and more convenient method of measuring and confirming the presence of A $\beta$ (1-42) in body fluids as compared to using laser desorption mass spectrometry.

#### ***Status of Claims***

7. All claims stand rejected.
8. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

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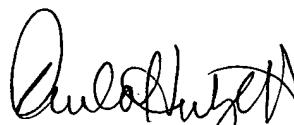
A) McConlogue et al (U.S. Patent No. 5,612,486) teaches screening assays in Swedish transgenic animals (i.e. a rodent model of amyloidosis) using biological specimens such as cerebrospinal fluid and brain homogenates.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy, Ph.D. whose telephone number is (703) 305-7555. The examiner can normally be reached on Monday-Friday from 6:30 AM to 3:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached at (703) 308-4310.

Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application should be directed may be submitted to Group 1800 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The FAX number for Art Unit 1818 is (703) 308-4242.

Patricia A. Duffy, Ph.D.  
May 11, 1997



PAULA K. HUTZELL  
SUPERVISORY PATENT EXAMINER  
GROUP 1800